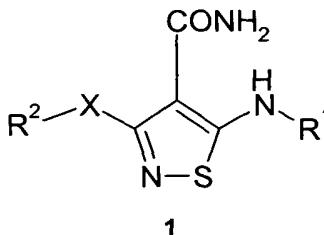


CLAIMS

1. A compound of the formula



- 5 or a pharmaceutically acceptable salt, prodrug, solvate or hydrate thereof, wherein:

X is O or S;

- R^1 is a 4-10 membered heterocyclic aromatic ring, optionally substituted with 1-4 R^3 groups, said R^1 group is optionally fused to a 4-10 membered aryl or heterocyclic group, said 4-10 membered aryl or heterocyclic groups are optionally substituted by 1 to 3 R^3 groups and 1 or 2 carbon atoms in the foregoing heterocyclic moiety are optionally substituted by an oxo (=O) moiety;

- R^2 is H, C_1 - C_{10} alkyl, C_3 - C_{10} cycloalkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, $-(CR^3R^3)_t(C_6$ - C_{10} aryl), or $-(CH_2)_t(5$ -10 membered heterocyclic), wherein t is an integer from 0 to 5; said alkyl group optionally includes 1 or 2 hetero moieties selected from O, S and $-N(R^5)-$ with the proviso that two O atoms, two S atoms, or an O and S atom are not attached directly to each other; said cycloalkyl, aryl and heterocyclic R^2 groups are optionally fused to a C_6 - C_{10} aryl group, a C_5 - C_8 saturated cyclic group, or a 5-10 membered heterocyclic group; 1 or 2 carbon atoms in the foregoing heterocyclic moieties are optionally substituted by an oxo (=O) moiety; the $-(CH_2)_t$ moieties of the foregoing R^2 groups optionally include a carbon-carbon double or triple bond where t is an integer from 2 to 5, and the foregoing R^2 groups are optionally substituted by 1 to 5 R^3 groups;

- each R^3 is independently selected from H, C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, $-OR^4$, $-C(O)R^4$, $-C(O)OR^4$, $-NR^5C(O)OR^4$, $-OC(O)R^4$, $-NR^5SO_2R^4$, $-SO_2NR^4R^5$, $-NR^5C(O)R^4$, $-C(O)NR^4R^5$, $-NR^4R^5$, $-S(O)_jR^4$ wherein j is an integer ranging from 0 to 2, $-SO_3H$, $-NR^4(CR^5R^6)_tOR^5$, $-(CH_2)_t(C_6$ - C_{10} aryl), $-SO_2(CH_2)_t(C_6$ - C_{10} aryl), $-S(CH_2)_t(C_6$ - C_{10} aryl), $-O(CH_2)_t(C_6$ - C_{10} aryl), $-(CH_2)_t(5$ -10 membered heterocyclic), and $-(CR^5R^6)_mOR^5$, wherein m is an integer from 1 to 5 and t is an integer from 0 to 5; said alkyl group optionally contains 1 or 2 hetero moieties selected from O, S and $-N(R^5)-$ with the proviso that two O atoms, two S atoms, or an O and S atom are not attached directly to each other; said aryl and heterocyclic R^3 groups are optionally fused to a C_6 - C_{10} aryl group, a C_5 - C_8 saturated cyclic group, or a 5-10 membered heterocyclic group; 1 or 2 carbon atoms in the foregoing heterocyclic moieties are optionally substituted by an oxo

EXPRESS MAIL NO. EL162816159 US

(=O) moiety; and the alkyl, aryl and heterocyclic moieties of the foregoing R^3 groups are optionally substituted by 1 to 3 substituents independently selected from halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, $-NR^5SO_2R^4$, $-SO_2NR^4R^5$, $-C(O)R^4$, $-C(O)OR^4$, $-OC(O)R^4$, $-NR^5C(O)R^4$, $-C(O)NR^4R^5$, $-NR^4R^5$, $-(CR^5R^6)_mOR^5$ wherein m is an integer from 1 to 5, $-OR^4$ and the substituents listed in the definition of R^4 ;

each R^4 is independently selected from H, C_1 - C_{10} alkyl, $-(CH_2)_t(C_6$ - C_{10} aryl), and $-(CH_2)_t$ (5-10 membered heterocyclic), wherein t is an integer from 0 to 5; said alkyl group optionally includes 1 or 2 hetero moieties selected from O, S and $-N(R^5)-$ with the proviso that two O atoms, two S atoms, or an O and S atom are not attached directly to each other; said aryl and heterocyclic R^4 groups are optionally fused to a C_6 - C_{10} aryl group, a C_5 - C_8 saturated cyclic group, or a 5-10 membered heterocyclic group; and the foregoing R^4 substituents, except H, are optionally substituted by 1 to 3 substituents independently selected from halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, $-C(O)R^5$, $-C(O)OR^5$, $-CO(O)R^5$, $-NR^5C(O)R^6$, $-C(O)NR^5R^6$, $-NR^5R^6$, hydroxy, C_1 - C_6 alkyl, and C_1 - C_6 alkoxy; and each R^5 and R^6 is independently H or C_1 - C_6 alkyl.

2. The compound of claim 1, wherein R^1 is a 5-6 membered nitrogen containing aromatic heterocyclic ring.

3. The compound of claim 2, wherein the 5-6 membered nitrogen containing aromatic heterocyclic ring is selected from the group consisting of 3-pyrazolyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrimidyl and 4-pyrimidyl.

4. The compound of claim 1, wherein R^2 is C_1 - C_4 alkyl, $-(CR^3R^3)_t(C_6$ - C_{10} aryl), or $-(CH_2)_t$ (5-10 membered heterocyclic).

5. The compound of claim 4, wherein C_1 - C_4 alkyl is methyl, ethyl or propyl.

6. The compound of claim 5, wherein the methyl, ethyl or propyl group is substituted by a cyclohexyl group.

7. The compound of claim 5, wherein said methyl, ethyl or propyl is substituted by a $-(CR^3R^3)_t(C_6$ - C_{10} aryl) group.

8. The compound of claim 4, wherein R^2 is $-(CR^3R^3)_t(C_6$ - C_{10} aryl).

9. The compound of claim 8, wherein R^2 is $-C(C_1$ - C_{10} alkyl) $_2(C_6$ - C_{10} aryl).

10. The compound of claim 9, wherein R^2 is $-C(H)(C_1$ - C_{10} alkyl)(C_6 - C_{10} aryl).

11. The compound of claim 10, wherein R^2 is $-C(H)(C_1$ - C_4 alkyl)(C_6 - C_{10} aryl).

12. The compound of claim 11, wherein R^2 is $-C(H)(C_1$ - C_4 alkyl)(phenyl).

13. The compound of claim 12, wherein R^2 is $-C(H)$ (methyl)(phenyl), $-C(H)$ (ethyl)(phenyl), or $-C(H)$ (propyl)(phenyl).

14. The compound of claim 13, wherein said phenyl moiety of R^2 is optionally substituted by 1 to 4 substituents independently selected from halo and C_1 - C_4 alkyl.

15. The compound of claim 8, wherein said $-(CR^3R^3)_l(C_6-C_{10} \text{ aryl})$ group is benzyl optionally substituted by 1 to 4 substituents independently selected from halo and C_1-C_4 alkyl.
16. The compound of claim 1, wherein X is S and R^2 is $-(CR^3R^3)_l(C_6-C_{10} \text{ aryl})$.
17. The compound of claim 16, wherein R^2 is $-C(H)(methyl)(phenyl)$,
5 $-C(H)(ethyl)(phenyl)$, or $-C(H)(propyl)(phenyl)$.
18. A compound according to claim 1 selected from the group consisting of:
3-Cyclohexylmethoxy-5-(pyrimidin-4-ylamino)-isothiazole-4-carboxylic acid amide
3-Cyclohexylmethoxy-5-(pyrimidin-2-ylamino)-isothiazole-4-carboxylic acid amide
3-cyclohexylmethoxy-5-(pyridin-2-ylamino)-isothiazole-4-carboxylic acid amide
10 3-Cyclohexylmethoxy-5-(3-methyl-pyridin-2-ylamino)-isothiazole-4-carboxylic acid
amide
3-Cyclohexylmethoxy-5-(pyridin-3-ylamino)-isothiazole-4-carboxylic acid amide
3-Cyclohexylmethoxy-5-(pyridin-4-ylamino)-isothiazole-4-carboxylic acid amide
3-Cyclohexylmethoxy-5-(1 H-pyrazol-3-ylamino)-isothiazole-4-carboxylic acid amide
15 5-(1H-Benzoimidazol-2-ylamino)-3-cyclohexylmethoxy-isothiazole-4-carboxylic acid
amide monoformate salt
3-(4-Chloro-benzylsulfanyl)-5-(pyridin-3-ylamino)-isothiazole-4-carboxylic acid amide
3-[1-(4-Chloro-phenyl)-propylsulfanyl]-5-(pyridin-3-ylamino)-isothiazole-4-carboxylic
acid amide
20 3-[1-(4-Chloro-phenyl)-ethylsulfanyl]-5-(pyridin-3-ylamino)-isothiazole-4-carboxylic
acid amide
3-(4-Chloro-benzylsulfanyl)-5-(pyridin-4-ylamino)-isothiazole-4-carboxylic acid amide
3-(2-Chloro-benzylsulfanyl)-5-(pyridin-4-ylamino)-isothiazole-4-carboxylic acid amide
3-(4-Chloro-benzylsulfanyl)-5-(6-methoxy-pyridin-3-ylamino)-isothiazole-4-carboxylic
25 acid amide
3-(4-Chloro-benzylsulfanyl)-5-(pyrimidin-4-ylamino)-isothiazole-4-carboxylic acid
amide
3-(4-Chloro-benzylsulfanyl)-5-(pyrazin-2-ylamino)-isothiazole-4-carboxylic acid amide
3-(2-Chloro-benzylsulfanyl)-5-(pyridin-3-ylamino)-isothiazole-4-carboxylic acid amide
30 3-(1-Phenyl-propylsulfanyl)-5-(pyridin-3-ylamino)-isothiazole-4-carboxylic acid amide
3-(4-Chloro-benzylsulfanyl)-5-(pyridin-2-ylamino)-isothiazole-4-carboxylic acid amide
3-(4-Chloro-benzylsulfanyl)-5-(pyrimidin-2-ylamino)-isothiazole-4-carboxylic acid
amide
3-(4-Chloro-benzylsulfanyl)-5-(6-methoxy-pyridin-2-ylamino)-isothiazole-4-carboxylic
35 acid amide

3-[1-(4-Chloro-phenyl)-propylsulfanyl]-5-(5-methyl-pyridin-2-ylamino)-isothiazole-4-carboxylic acid amide

3-[1-(4-Chloro-phenyl)-propylsulfanyl]-5-(6-methyl-pyridin-2-ylamino)-isothiazole-4-carboxylic acid amide

5 3-[1-(4-Chloro-phenyl)-propylsulfanyl]-5-(3-methyl-pyridin-2-ylamino)-isothiazole-4-carboxylic acid amide

3-[1-(4-Chloro-phenyl)-propylsulfanyl]-5-(6-methyl-pyridin-3-ylamino)-isothiazole-4-carboxylic acid amide

and the pharmaceutically acceptable salts, prodrugs and solvates of said compounds.

10 19. A pharmaceutical composition for the treatment of a hyperproliferative disorder in a mammal which comprises a therapeutically effective amount of a compound according to claim 1 and a pharmaceutically acceptable carrier.

20. The pharmaceutical composition of claim 19 wherein said hyperproliferative disorder is a cancer selected from brain, melanoma, lung, squamous cell, bladder, gastric, 15 pancreatic, breast, head, neck, renal, kidney, ovarian, prostate, colorectal, oesophageal, gynecological and thyroid cancer.

21. The pharmaceutical composition of claim 20 wherein said disorder is a non-cancerous hyperproliferative disorder

20 22. The pharmaceutical composition of claim 21 wherein said disorder is a benign hyperplasia of the skin or prostate.

23. A method of treating a hyperproliferative disorder in a mammal which comprises administering to said mammal a therapeutically effective amount of a compound according to claim 1.

25 24. The method of claim 23 wherein said method is for the treatment of a cancer selected from brain, melanoma, squamous cell, bladder, gastric, pancreatic, breast, head, neck, oesophageal, prostate, colorectal, lung, renal, kidney, ovarian, gynecological and thyroid cancer.

25. The method of claim 23 wherein said method is for the treatment of a non-cancerous hyperproliferative disorder.

30 26. The method of claim 25 wherein said method is for the treatment of a benign hyperplasia of the skin or prostate.

27. A method for the treatment of a hyperproliferative disorder in a mammal which comprises administering to said mammal a therapeutically effective amount of a compound according to claim 1 in combination with an anti-tumor agent selected from the group consisting 35 of mitotic inhibitors, alkylating agents, anti-metabolites, intercalating antibiotics, growth factor inhibitors, cell cycle inhibitors, enzymes, topoisomerase inhibitors, biological response

modifiers, anti-hormones, NK1 receptor antagonist, 5-HT₃ receptor antagonist, COX-2 inhibitor, an EGFR inhibitor, and anti-androgens.

28. A method of treating pain in a mammal which comprises administering to said mammal a therapeutically effective amount of a compound according to claim 1.

5 29. A method of treating obesity in a mammal which comprises administering to said mammal a therapeutically effective amount of a compound according to claim 1.

30. A method of treating neuropathy in a mammal which comprises administering to said mammal a therapeutically effective amount of a compound according to claim 1.